

### REMARKS

Claim 1 has been amended to clarify that the cells that produce a first fluorescent protein are separated microscurgically from cells that do not produce said first fluorescent protein. Support for this amendment is found, for example, on page 5 of the specification in paragraph 15, first part of the third sentence. Claim 3 has been canceled as redundant and claim 4 has been canceled as not in accord with the method now being claimed. Claim 8 has been amended simply to correct an inadvertent error in its dependence and claim 9 has been amended for clarification in response to the rejection under 35 U.S.C. § 112, paragraph 2.

No new matter has been added and entry of the amendment is respectfully requested.

#### Rejection Under 35 U.S.C. § 112, Second Paragraph

This rejection of claim 9 has been addressed by amendment. The objected-to phrase “portions of said cells” no longer appears in the claim.

#### Rejection Under 35 U.S.C. § 102

Claims 1, 3-4, 6-7, 10 and 11 were rejected as assertedly anticipated by Hadjantonakis, *et al.*, *Histochem. Cell. Biol.* (2001) 115:49-58.

This rejection, too, has been addressed by amendment. Claim 1 now requires that the cells that produce a first fluorescent protein be microscurgically separated from those that do not. This procedure is not used by Hadjantonakis as shown in Figure 4 thereof. The only manual dissection of cells results in a mixture of cells that produce a fluorescent protein and those that do not. Any separation of the cells that produce the fluorescent protein from those that do not is by FACS analysis. This procedure is no longer being claimed.

Applicants recognize that claim 3 has been included in this basis for rejection, but believe that that inclusion was in error in that the separating of cells is not just separating from a tissue, but also separating fluorescent protein producers from non-producers by surgical procedures. Hadjantonakis does not do this. Therefore claim 1 is novel.

Claim 4 has been canceled; claims 6-7, 10 and 11 depend from claim 1 which is not anticipated and thus this basis for rejection is obviated as well.

#### Rejection Under 35 U.S.C. § 103

All claims were rejected as assertedly obvious over the combination of Hadjantonakis in view of Rashidi, *et al.*, *Clin. Exp. Metastasis* (2000) 18:57-60. The Rashidi document is added for the purpose of showing that the cells producing the first fluorescent protein can be tumor cells and can be manipulated through surgical orthotopic implantation.

This basis for rejection may be withdrawn for the same reasons that the rejection for anticipation can be withdrawn – *i.e.*, the primary document does not describe the claimed procedure with respect to any kind of cells. The secondary document does not remedy this defect.

In addition, applicants point out that the method of the invention is highly advantageous because as microsurgical techniques can be used to remove labeled cells from a particular location in a tissue, the location of the cells removed can be recorded and additional information provided as to the nature of the cells at particular locations. This permits a study of, for example, heterogeneity of a tumor. Such a possibility is not available in the procedure set forth in the primary document.

Thus, applicants believe that the claims as amended are not rendered obvious by the combination of Hadjantonakis and Rashidi.

Conclusion

Claim 1 has been amended to clarify that the invention is now directed to microsurgically separating labeled from unlabeled cells at a location in a tissue. There is no document of record which describes such a procedure. Thus, applicants believe that the pending claims, claims 1-2 and 5-11, are in a position for allowance and passage of these claims to issue is respectfully requested.

If minor wording issues remain that could be resolved in a telephone conversation, a call to the undersigned would be appreciated.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 312762004100.

Respectfully submitted,

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